

CLAIMS

*Sub D*  
1. A method of screening and recovering a regulatory DNA capable of inducing metastasis comprising the steps of:

i. transferring tagged fragments of a human DNA from malignant, metastatic cancer cells into a cell line that produces only benign, non-metastasizing tumours when injected into a syngeneic animal;

ii. injecting the transformed cells into the syngeneic animal;

iii. selecting those animals in which metastasizing tumours have been identified; and

iv. recovering the regulatory DNA capable of inducing metastasis therefrom.

2. A method as claimed in claim 1 in which the fragments of human DNA transferred in step 1 are from 0.1 to 50 kilo base pairs in length.

3. A method as claimed in claim 2 in which the fragments of human DNA transferred in step (i) are less than 1.6 kilo base pairs in length.

*Sub A*  
4. A method as claimed in claim 1, 2 or 3 in which the cell line that produces only benign non-metastasizing tumours is a rat mammary epithelial cell line.

5. A method as claimed in claim 4 wherein the rat mammary epithelial cell line is a Rama 37 cell line.

6. A method as claimed in claim 5 wherein the tag is an oligonucleotide sequence:

Primer

5' AATCCAAGCTTGCGGCCGATCAGGCCGAATATGCGGCCGCATTAT-3'  
AGGTTCGAACGCCGGCTAGTCCGGCTTATACGCCGGCGTAATATCGA

HindIII

SfiI

NorI

Defective  
HindIII

*Sub  
D's*

7. ~~A regulatory DNA capable of inducing metastasis consisting essentially of a human DNA fragment of less than 1.6 kilobase pair in length obtained from a malignant, metastasis cancer cell.~~

8.  DNA consisting essentially of a regulatory DNA capable of inducing metastasis from sequence 1:

C2

CTTCCTTGGT	GCTCTATGTC	TTGCCTCTCC	CCTTCTCCAG	TCCCATTAAAG	CCATAACCAT
CTTGACAGAC	TCTGGGACAG	TCCCCTCTGC	TCTCCTGTTG	GCGCCTGAGT	CCCTTTTTCG
CTGAGGACCC	TTCACGTAGC	CTCCCATCTG	GATGACCTAG	TAGAAGACGT	GGGAAGTTGT
CACACTCAGG	TAACTGAGCA	GAGCTCAGAG	ATTTAAAGTC	AGTCTGGGA	GCCTCGAGGA
TTGATCTGCT	GCCTTAAAAAA	GCCAATTGGA	TGACTAACCC	AGACTATTGT	CACTTTAGGT
GGGAAGTCAC	TAGCATATCT	GATGGGTACAC	ATCTGAGAAA	GTTTCTAGC	AGTGGTGGCC
TTGTGTGAGC	AGCATGGCGT	GTATCATGGT	GTGCAGCATA	CTCAGGCTGC	TTGCACACCT
CGAGGCTCTT	CTTCAGTATT	AGGGGACCA	CTGGTGTTSG	AACATGGTCC	AAGPATAACAG
TCATGTGAGG	AGAATCCAA	TGCGTCAGGA	GAIAACCGAGA	GTCTGTGACC	TCCATTCTTC
AAAGATACAGA	ATTATTCTTG	GACTGTGTTT	TCATGCTCCT	TGTGGATCGG	AGTGAGTTA
CTTCAGGTTA	ATCAGCATTC	CTTACTGTTG	GTATTCAAGT	AAATGCTAA	ATTATCCTGG
ATATAACCTCT	GTGGGAGCA	GGTTTTTGAT	ACATGCCAGCT	TGTCTTGTG	ATTGTTACTG
CTTGAACCTCA	AGAGAACTTT	GCTCATGTGA	TCTTCTTAA	CCGATGGAGT	AGAAACTGTC
TGATGCTCTC	AATAAAGTTG	GCTCTTGCAC	GAGACGTTAG	TCTGTCTGT	TTATCTGCTC
CATTCTTCCG	CTCCCACGGC	CTCTACAGCA	CTAAACCCAC	CACCGATAGA	CTCAGTCTT
CACTGACAAA	CATCACCAAGA	GGCTCTTAAC	TGAGATTATA	AACTGTTACT	AGATGATGGG
TGGIATCGCT	CCCCAGAAC	ATTAACATT	ACTTGGAGAA	CTCAAGACCC	CTTTGTAGAC
ATAACTCCCCA	TGGT				

9.  DNA consisting essentially of a regulatory DNA capable of inducing metastasis from sequence 2:

C5

ATGCTGTGA	GCCTATTAGC	GACATTTGGT	GACGCCCTT	TTAAGGGGT	AGATACAAAG
AATGGGTTGA	AATTCTGTGC	CACAAACGCT	CTCCATGTT	TCACAATTAC	ACTTGCAACC
TGTGGTCAGC	AGCCAGAATT	TAGGGATGTG	ATGGGACAGG	GTCCGGGAAA	GAAGGAGAAG
GGTAAGGAA	AGACAGCAGC	TTAAGTCCA	AACAGCTCCA	GGAGACTATC	TGTAGAAATA
ACATCAGACC	ATGAGGAGAA	TTGATATCAT	TGTTTTCTAA	TGGGTATCGC	CAACGGAACT
TTCCATCTGA	TTAATATCAA	TTACTGCTGG	CACTAAATCC	AATTGGAAAT	GCCCCACACA
ATTATCTTC	CACTTCATGC	TGCTACCATA	TGCCTGACGT	GGCGGAGCAG	AAGCATTCCC
TCCC GTTCTG	ATAAATAGTA	CTTTGTAAT	ATTGGAGAC	GGGAGCTCTG	GTGACAGGGA
ACACGTACAA	ACCGGCCTGT	TTATCATGTT	CCCGATAGAG	GCCCTCTTTC	ACGTACAGGA
CCCCAAACAA	GTCAGGATGC	TGTGAATTTC	CTTCCATGAA	GCCTTGTTC	CAATTAGCAA
CCATTGGAGG	AAGCAGGCTG	CACTGTCTAC	CACAACTGGC	ACTTTCCAAA	GAGCACACAT
ATATTGGAGC	AAGACATTTC	GCTGGCTGAC	TGGTGCTGTG	TAAGCTGATA	AACTGCTATA
TTTATTAAC	TGGCTTTCT	TTGAAACACC	CACTCAAGGA	APPAAAACA	CACTTAGGGT
GACATTATT	GGAGATGAAG	TCTTTATAGA	GATGCTTAAG	TTTAAACGAG	ACTTTAAAG
CCGGCTCTAT	TCCATTAAAT	GAATGGTGTG	CCTACAAAGG	AAGAAACTGG	GACAGAGGTA
TGTRACACTTG	TGTGTGTGTC	AGAGACAAAC	TGAGGAGCTG	AAGAGGACCA	CGTACAAAGTC
AGAGAAAGGC	TGACCCATTAT	TCACACTGAG	CAAAACCAGTC	ATGTGTGGGT	CGATAGATGA
CACTATCCCC	CAAGACTCAC	ACATTGCAAC	GCTTGCTC		

10. ✓ DNA consisting essentially of a regulatory  
DNA capable of inducing metastasis from sequence 3:

C6

AGGACCAGAG TTCACATCCC ATCAATTGGC CCAGAAGGTT TTAATGCTGT CTTTGCCCC  
ACGGGGCGAAC TGCACACACA TGTGCACATA CACTTACAGA GACACACATT CAGCAGCATA  
AGAACACAAAT CACAAATAAA AAAAATCTTG AAAAATTTTA AGCTAAAATT GTTAAGAAAT  
AACATATATA CAATTTTCT TTATTTTTT AAAAGATTAT TTATTTAATG TATATGAGTA  
CACTGCCTCT CCCTCCAGAC ATAGCACTAC AGGGCATCGG ATCCCATTAC AGATGGITGT  
GAGCCACCAT GTGGTTTCAC AGATGGTTGT GAGCCACCAT GTGGTTTCAG GAATTGAACT  
CAGGACCTTT GGAAGAGCAG TCAGTGCTCT TAACCTCTAA GCCATCTCTC CTGACCCCTA  
TATACAAATT TAATGCTACG TACACACAAAC TTCTCTTCC TTTAATGGTT GAGATTTTG  
TCTGGAGAAG TAAGATAAA GGAGGGAAAG AACATTGCTT TCACATTGCA CCAGTGGGAA  
CAGCGTGTTC AAGCTAGGA TGCCATGAAA TGACTGGCCT GCCTTCTCAT TACTGTCCT  
CCCACTCCTC CTTTAACTG GAGCTCCTT ATCTAATTAA TTAGTTGAC GATACCCAGG  
GTTTTCTTCT GTTTGATCT TTTTAAGACA GAGACTCACC ATATAGCCCT GGCTGGCCTG  
AAGCTCACTA TGTAGACCAAG TCTGGCCTTG AACTCAAAGG AGATCTATCT GCTTCCTAGT  
GCTGGGATTA AAGGCTTGTG CTACCAAGTC TGGTCTGAGG CTTTGGAGCA GCCTCGGTAA  
TGGCCTTCTT TAAGGATCTC TAAGCTAGCA GTTAAGTAGCC TAGCCATGCT GTTGTAGGAA  
GTTGTTCGTT CATCCTGGCT CCAGCACAAA GGCAAGTCACT AAACGTGGC CTCATTTCAT  
CAGAGCTGAA TGCATAATTCC TTGTGCTCTT CCTGTGTCCT CCTGGAAC

✓ 11. DNA consisting essentially of a regulatory  
DNA capable of inducing metastasis from sequence 4:

C9

AGTTGGGGAC ACAGCTTGCT TGATTAAGAT GTTCTTGGG AAAAAGGAGTT AAGCCTAATG  
ATTTCCAATG GAAAGGACTG CTAATTGGG AGCAATGTT GCTTAATTGG GACACCTGCG  
GGTAAATTAAA AGCTCTCTCC CAGTGGCCTT TCCTGTTTT GGCTCTGGG GGCAGAGGCA  
TTGAGAGGGA TCCAGGCATT CTAAGGGCTG GTTCTTGGTT TCTCCCTTCC CCTCTGTCCA  
AACTCACTCA GGTATCCCTG TCTGTGCTGT CCTTAGAGTG CCGTCCTGAG GCCTGGTCA  
GTTAAGGTCT CTGGATCTGA GCTGCCCTAG GGAAACGGCAT GAGCTCATG GAAAGGGAG  
AACCAAGCAA AGGTGTTGGC TGTGACCTCA GAATTCTGAG GGGCAAGGT TCAAGGCTAA  
CTCTCATTAT AGAGCAAGTT TGAGACTGGC CTGGGAACAA AAATATAAAG TGAGTGGAGGT  
CATATGACAG CACCTGAGGA GTCCTGTCCC TAGAGATCAT AAGGACCTGG CTGCTGGGAA  
CTTGTGCAAG ATGGCACTTT GTGTGAGAG AGGGGACCTG CCCAGGATG CGAGGCCCTG  
GAAGATCCTC TGGATTAACT GTGAAACACTG ATTGCTGCTT TATACTGGG TTTGTGCTGT  
TATCTGGTAC ACATCTGTC GGTGAATGAG TTCAATGGCT TTATTTCACT GAGGTATTTA  
CCTGAGGAGA AAGAAGGACT GGTGCCACAA AGCACAGCTT TTAAATCTGT GGTTGTGAC  
CCATTATGGA CTATCATAAC TGAGTGCAGG TATCAAGAAT ACTTTAGCAG GTGGTAAAAA  
GATTTTGAA TGGCAACGA CCAAAACTGA ACTCAAAAT CAAGCATGGC ATGGATCCTG  
GGTGTCTCTG GAAGCACTTG CCTTTACTGC ATTGTGCGAC TTGACGGTAG CCTTGTTCT  
GAATGCAAA CACGTGGGCT TTGGGCTGCA CAGGCCACCA CGCCGTGCCT GAAACACCTC  
AGCTCAGGTT TGTGGCTATG TCCTATGACT TGGACTTACT TTTATTGCAC ATATTAATAT  
TTTCCTGCA

12 ✓ DNA consisting essentially of a regulatory  
DNA capable of inducing metastasis from sequence 5:

C12

GAGGGGGTGG TGGCACAGTT ATGTTTTGT AGGAAGGGTT CCATGAACCT CAGCAGAGCT  
CGGGTTAGAA ATTAAAGC CCTGAGGGAA ATTTTTTTTT TAAATCGCTA TGAATCTGAC  
ATGAGAAATAA CAAGATCAGAA ACGTTCTTGT GCTTCAGAAA AGGACAAGTG TGTGAGCTAA  
CAGACTGCAC ACTGGTGTTC GAGGCACATC TGGATCACAG GAGCGTCAGA TAAATGCCCC  
AAAGGTAAT GCATTGCTT GCACAGTACC GAGTGTGGTG GGGGTCCT ACAGCCCAAGC  
GGTTCTCAAC CTTCCTGATG CTTCGACCCCT TTAATAACAGT GCCTCATGCT CTGGTACACCT  
CCCCAACCTT AAAATTATTT TTGTTGCTGT TCATAACTGT GATTTGATA CTGTTATGAA  
TTGTAATATA AATAATTTG AAGAAAGAGG TTTGCCAAGG GTTGAAGAAC TGCTGTTCTA  
CCCCACGTG GATGGTTTT CGTCATTGCG GGTTTTATG AGGCAGAGTC TTATGTAGCC  
CAGGCTAGCA GCCTAGAATG TGCTACTTAG CTGAGGAATA ACCTTGGAAC TTCTGAGGAC  
TGGAGAGACT GGCTTAGTCC TCAAGAAACT GGAATAAGCT GGAGTTGGC TACTTGTGGG  
TTCCTTTTC TTCAAACCTT TTCTACTCTT TTTCCACCCCT GTCGGCCCCC TAAACACTAAA  
TAAGAAAGAG AAAGGGGAGC ATAGAGGGAA AAAGAAACCC CTGAATAACG TCAGTAGTTG  
GCAAAGGGGG GTGACATATG TTGTCATTAG ACCACATCCT GGTGATTAAG GGGAGTCAAG  
TTCCTTGGGG CAAGTTTGAT CTTCGTGTAA ACGATATCTA ATTTCTTCTC CCTGTTGCTT  
CGTCTTGTG AACAAACGACT TGATAACCCA CAATGGACCA TCAACCAACC AACCAACCAT

13 ✓ DNA consisting essentially of a regulatory  
DNA capable of inducing metastasis from sequence 6:

C20

TTGTCTCTGG TGTTACTTGT TTTCCATTCT CGACAGTGG TTTGACCTT CTATACGCCCT  
GTGTGTCAAG AGTGTGTAG ACCTATTTC CTGTTTCTT TCAGCCAGTT ACAGGAACAG  
AGTGTCTAC TGTCAAGATGT GTACCTGTT CTGTCACCTG ACTTTCAAGC TGTCTCTGTG  
TGCAGGAACC AGAAGGGCCT GTCCCTACTT CTACTGGCC CCTACGCACA GGGGGCTAG  
ATGGTCTAG GTGTTTCCT CTAGAGCCTG AAATGTGGGC AGAGAGTAGT CTCCTCTGGT  
TTCCTAGGTA TGTCTTCCCC TCTGAAGGTC TAGCTCTCCC TTCCATGGGAA TATGGGTGCA  
GGGAGCTGTT TGACCAAGGTC CTCTCAAAATC CGGGTGCAGT CTGGACCGCA GGCTCCTGTA  
GCTTGCCTGC TGCAATCTTC CCGCACCCAG AGGCACCCAA GTTTCCTCTT GGGCCAGGA  
TGTGGGCAAA GGTGGGCAGA ACTGGCAATC TCTCCTGCCCT TAGCGTCTCA CGATTGCCCT  
CACTTCTGGG CAATCCGCTC TCTCTTCCAC AGGGTTGGG AGCAGGGAGC TGTGGGCCGG  
TATCAGGCAA AGGTTTGAGG CAACCAAGTTA GAAACTGGAA GTGTCAAGTC CCAGAGGAAT  
TTTGCCTTG TGTGTCTGA GTCCACCAAGG CAGGTCACTT GGAGCAAGAA AATTGGTTT  
CCCCTCGTC TCAAGGCCTGA AGTGTGCACCT CAGGGTTGGC TTTCAGCTGT ACCTGTGGAA  
AGTATGGTT TAAAAATCTA AGATAGCTAT CATGCAGCAA GGCTGTGTA AAATGTCTAT  
TTGGTTCTT TATGACTTAC TTTGCTGTA CTGAGGATCA AACCTAGGGT CTCAAGGAGT  
CATCACCAATT CTCTGTCACT GATCCAGCTC CATTCTATT TTCTTTGTC CGCGCGGATC  
TCTCGCCAGC AAGAAACAC GCTAGGGACA TACGAATCCT TGCTGCAGCC AAAACTTTA  
TTGAATCTTA AGGAGAAGCC CGCGCACCGG ACTGGCGCCGG TTTATATCA CCCTAGCA  
GTCCATCCAC A

14 ✓ The use of an osteopontin gene as a  
metastasis inducing transformant.

*Sub Q2* 15. A probe specific to a regulatory DNA capable of inducing metastasis as claimed in any of claims 7 to 13.

*Sub Q1* 16. A kit for diagnosing the likelihood of a cancer metastasizing comprising a probe as claimed in claim 15 and one or more of a colour indicator, an oligonucleotide primer, materials for gel analysis and materials for DNA transfer or hybridisation.

*Sub Q3* 17. A medicament adapted to target a regulatory DNA capable of inducing metastasis as claimed in any of claims 7 to 13.

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